REMARKS

STATUS OF THE CLAIMS

Claims 1-59 are now pending in the present application, Claim 1 having been amended to correct an error and new Claims 2-59 having been added by the present amendment.

The Examiner is requested to consider the application in the light of the present amendment. In the event that any issues arise during the course of such consideration, the Examiner is invited to telephone applicants' attorney at the number listed below.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the U.S. Postal Service in a sealed envelope as first class mail with postage thereon fully prepaid addressed to: Commissioner of Patents and Trademarks, Arlington, VA 22202, on August 28, 2002.

Kathy L Pauline

Date: August 28, 2002
RMA:MCK:klp

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MARKED-UP VERSION OF THE AMENDMENTS

AMENDMENT TO THE CLAIMS

In the Claims:

Please amend Claim 1 as follows:

1. (Amended) A method for imaging and decoding a plurality of encoded beads comprising the steps of:

(a) collecting light from an encoded bead along a collection path;

(b) dispersing the light that is traveling along the collection path into a plurality of light beams, as a function of a plurality of different discriminable characteristics of the light;

(c) focussing each of the plurality of light beams to produce a respective image corresponding to that light beam, thereby generating a plurality of images, each image being indicative of an identity of said encoded bead;

(d) detecting the plurality of images;

(e) analyzing the plurality of images to determine the identity of said encoded bead; and

(f) repeating steps (a)-(e) for successive encoded beads from the plurality of encoded beads.

Please add new Claims 2-59 as follows:

--2. The method of Claim 1, wherein the step of dispersing comprises the steps of dividing the light into the plurality of light beams as a function of a wavelength.

3. The method of Claim 1, wherein the step of analyzing the plurality of images comprises the steps of generating a plurality of signals, each signal thus generated indicating the presence of a different discriminable characteristic of the light.

4. The method of Claim 1, wherein the step of analyzing the plurality of images comprises the step of constructing a sequence library based on each encoded bead that is decoded.

5. The method of Claim 1, further comprising the step of illuminating the plurality of encoded beads with light while the encoded beads are moving.

6. The method of Claim 1, wherein the step of analyzing the plurality of images comprises the steps of:

(a) determining dispositions of reporters associated with the bead;

(b) determining a signature of each reporter associated with the bead based upon the dispositions of the reporters in the plurality of images collected from each encoded bead; and

(c) decoding each bead as a function of each signature associated with the bead.

7. The method of Claim 1, further comprising the step of providing redundant reporters for each encoded bead.

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8. The method of Claim 1, further comprising the step of disregarding the identity of an encoded bead if the plurality of images for that encoded bead indicate that fewer than a predetermined number of reporters are associated with the encoded bead.

9. The method of Claim 1, wherein the step of analyzing comprises the step of referring to an encoded bead legend that identifies each encoded bead as a function of optically discriminable reporters associated with each encoded bead.

10. The method of Claim 1, further comprising the step of disregarding the identity of each encoded bead if the analysis of the plurality of images determined that an encoded bead has not experienced a binding event.

11. The method of Claim 1, wherein the step of analyzing comprises the step of de-convolving the images if the step of dispersing convolves the plurality of light beams.

12. The method of Claim 1, wherein the step of dispersing comprises the step of providing an image corresponding to a binding signal produced by the encoded bead.

13. A method for imaging a plurality of encoded beads entrained in a flow of fluid to identify a compound attached to each encoded bead, corresponding reporters attached to each bead identifying a unique bead signature, thereby identifying the attached compound, said method comprising the steps of:

(a) providing an imaging system for imaging encoded beads contained within the flow of fluid, said imaging system including at least one light source for illuminating an encoded bead within the flow of fluid passing through the imaging system;

(b) focussing light from the encoded bead along a collection path that is in a direction not aligned with the flow of fluid;

(c) dispersing the light that is traveling along the collection path into a plurality of light beams, as a function of a plurality of different discriminable characteristics of the light, said plurality of different discriminable characteristics being indicative of an identity of each reporter that may be attached to the encoded bead;

(d) focussing each of the light beams to produce a respective image corresponding to that light beam;

(e) detecting respective images thus produced;

(f) generating a plurality of signals based on the respective images, each signal identifying those reporters present on each encoded bead;

(g) analyzing each respective image to determine the identity of each reporter present on each encoded bead, thereby identifying the compound attached to that bead; and

(h) repeating steps (a)-(g) for successive encoded beads in the flow of fluid.

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14. The method of Claim 13, wherein the step of analyzing each respective image comprises the steps of:

(a) determining a signature of each reporter associated with the encoded bead based upon the locations of the reporters on the bead; and

(b) identifying the compound as a function of each reporter associated with the encoded bead.

15. The method of Claim 13, wherein the step of analyzing comprises the steps of disregarding images relating to a reporter if an image from an identical reporter have already been analyzed, and disregarding all images for an encoded bead if said images indicate that fewer than a predetermined number of reporters are associated with the encoded bead.

16. The method of Claim 13, wherein the step of analyzing comprises the step of referring to an encoded bead legend that relates each unique set of reporters to a specific compound.

17. The method of Claim 16, wherein the step of analyzing comprises the step of disregarding all images for an encoded bead if it is determined that the encoded bead does not correspond to said bead legend.

18. The method of Claim 13, wherein the step of analyzing comprises the step of de-convolving the images if the step of dispersing convolves the plurality of light beams.

19. The method of Claim 13, wherein the step of dispersing comprises the step of providing an image corresponding to a binding signal produced by the encoded bead itself.

20. The method of Claim 19, further comprising the step of disregarding all signals for an encoded bead if any image relating to that encoded bead indicates that the encoded bead has not experienced a binding event.

21. A method for simultaneously imaging a plurality of reporters disposed on substantially different portions of an encoded bead to identify each unique reporter included on the encoded bead, said method comprising the steps of:

(a) receiving light from the encoded bead along a plurality of collection paths that are substantially spaced apart, such that light from the reporters disposed on the different portions of the encoded bead affect the light received therefrom; and

(b) processing the light received from the encoded bead along the plurality of collections paths to identify each unique reporter included on the encoded bead.

22. The method of Claim 21, further comprising the step of providing redundant copies of each unique reporter on the encoded bead.

23. The method of Claim 21, further comprising the steps of reducing the number of unique reporters necessary to encode a bead; and selecting a library to encode a bead characterized by a length between 9-mer and 16-mer.

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24. An imaging system for imaging and decoding a plurality of encoded beads to which is attached one or more compounds, each compound being associated with a unique reporter set , each reporter set including at least one reporter, comprising:

(a) a collection lens disposed so that light traveling from each encoded bead passes through the collection lens and is focussed along a collection path;

(b) a dispersing component that receives the light from the collection lens and disperses the light into a plurality of light beams, as a function of a plurality of different discriminable characteristics of the light, said plurality of different discriminable characteristics being indicative of the reporter sets associated with the encoded beads;

(c) at least one pixilated detector;

(d) an imaging lens that focuses each of the plurality of light beams on said at least one pixilated detector, producing a respective image corresponding to each of the plurality of light beams, said at least one pixilated detector providing an output signal for each respective image, each output signal indicating the reporter set associated with the encoded bead; and

(e) a signal processor coupled to receive the output signals from said at least one pixilated detector, said signal processor processing the output signals to decode each reporter set associated with the encoded bead, thereby identifying each compound attached to the encoded bead.

25. The imaging system of Claim 24, wherein said signal processor is adapted to generated sequence contigs from a plurality of decoded beads.

26. The imaging system of Claim 25, wherein said sequence contigs identify at least one of a genomic DNA sequence, a polymorphic allele, and an expressed gene.

27. The imaging system of Claim 24, wherein said signal processor is adapted to analyze said output signals to:

(a) determine dispositions of the reporters on the encoded bead;

(b) determine a signature of each reporter associated with the encoded bead based upon the dispositions of the reporters on the bead; and

(c) determine a reporter set associated with the encoded bead based upon the reporter signatures; and

(d) identify the each compound associated with the reporter set.

28. The imaging system of Claim 24, wherein said signal processor is adapted to disregard all output signals relating to a reporter if signals from an identical reporter have already been analyzed, and to disregard all output signals for an encoded bead if said signals indicate that fewer than a predetermined number of reporters are associated with the encoded bead.

29. The imaging system of Claim 24, wherein said signal processor is adapted to employ an encoded bead legend that relates each unique reporter set to a specific compound.

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30. The imaging system of Claim 29, wherein said signal processor is adapted to disregard all output signals for an encoded bead if it is determined that the encoded bead does not correspond to said encoded bead legend.

31. The imaging system of Claim 24, wherein said signal processor is adapted to de-convolve the output signals if said dispersing component convolves the plurality of light beams.

32. The imaging system of Claim 24, wherein said dispersing component provides one respective image corresponding to a binding signal produced by the encoded bead.

33. The imaging system of Claim 32, wherein said signal processor is adapted to disregard all output signals for an encoded bead if said one respective image indicates that an encoded bead has not experienced a binding event.

34. The imaging system of Claim 24, wherein said dispersing component comprises one of a dichroic filters and a prism.

35. The imaging system of Claim 24, wherein said at least one pixilated detector comprises a time delay integration (TDI) detector.

36. The imaging system of Claim 24, wherein said imaging lens focuses each one of said plurality of light beams onto a different region of said at least one pixilated detector.

37. A flow imaging system for sequentially imaging and decoding a plurality of encoded beads entrained in a fluid, said encoded beads comprising one or more compounds from among a plurality of different compounds, and one or more reporters from among a plurality of different reporters, each different compound being uniquely identified by at least one reporter, said flow imaging system comprising:

(a) at least one light source for illuminating an encoded bead within a flow of fluid passing through the flow imaging system;

(b) a collection lens disposed so that light traveling from an encoded bead passes through the collection lens and travels along a collection path;

(c) a dispersing component that receives the light from the collection lens and disperses the light into a plurality of light beams, as a function of a plurality of different discriminable characteristics of the light, said plurality of different discriminable characteristics being indicative of the plurality of different reporters;

(d) at least one pixilated detector;

(e) an imaging lens that focuses each of the plurality of light beams on said at least one pixilated detector, producing a respective image corresponding to each of the plurality of light beams, said at least one pixilated detector providing an output signal for each respective image, each output signal identifying those reporters present on the encoded bead; and

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(f) a signal processor coupled to receive the output signals from said at least one pixilated detector, said signal processor processing the output signals to decode those compounds present on the encoded bead, based on the identity of those reporters present on the encoded bead.

38. The flow imaging system of Claim 37, wherein said at least one pixilated detector comprises a time delay and integration (TDI) detector.

39. The flow imaging system of Claim 37, wherein said signal processor is adapted to analyze said output signals to:

(a) determine a signature of each reporter associated with the encoded bead based upon a locations of the reporters on the bead; and

(b) identify the compounds as a function of each reporter associated with the encoded bead.

40. The flow imaging system of Claim 37, wherein said signal processor is adapted to disregard all output signals relating to a reporter if signals from an identical reporter have already been analyzed, and to disregard all output signals for an encoded bead if said signals indicate that fewer than a predetermined number of reporters are associated with the encoded bead.

41. The flow imaging system of Claim 37, wherein said signal processor is adapted to de-convolving the output signals if said dispersing component convolves the plurality of light beams.

42. The flow imaging system of Claim 37, wherein said dispersing component provides one respective image corresponding to a binding signal produced by the encoded bead itself.

43. The flow imaging system of Claim 42, wherein said signal processor is adapted to disregard all output signals for an encoded bead if said one respective image indicates that an encoded bead has not experienced a binding event.

44. A flow imaging system for sequentially imaging and decoding a plurality of encoded beads entrained in a fluid, said encoded beads comprising one or more compounds from among a plurality of different compounds, and one or more reporters from among a plurality of different reporters, each compound being uniquely identified by at least one reporter, said flow imaging system comprising:

(a) a collection lens disposed so that light traveling from an encoded bead passes through the collection lens and travels along a collection path;

(b) a plurality of light reflecting elements disposed in the collection path, each light reflecting element reflecting light of a different predefined characteristic, and passing light that does not have that predefined characteristic, the reporters on an encoded bead determining the characteristics of light traveling along the collection path, each light reflecting element being positioned at a different location with respect to the collection path to reflect light of a specific predefined characteristic in a direction different from that of other light reflecting elements, each light

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reflecting element being positioned along an axis of said collection path, such that passing light not reflected by a preceding light reflecting element reaches a last light reflecting element;

(c) at least one pixilated detector disposed to receive light that has been reflected by each of the light reflecting elements, said at least one pixilated detector comprising a plurality of pixilated regions, each pixilated region producing an output signal that is indicative of at least one characteristic of the encoded beads and thus indicative of the reporters; and

(d) a signal processor coupled to receive the output signals from said the plurality of regions, said signal processor processing the output signals to decode an identity of the compounds as a function of the reporters present on the encoded bead.

45. The flow imaging system of Claim 44, wherein said plurality of light reflecting elements comprise dichroic filters.

46. A flow imaging system for sequentially imaging and decoding a plurality of encoded beads entrained in a fluid, said encoded beads comprising one or more compounds from among a plurality of different compounds, and one or more reporters from among a plurality of different reporters, each compound being uniquely identified by at least one reporter, said flow imaging system comprising:

(a) a collection lens disposed so that light traveling from an encoded bead object passes through the collection lens and travels along a collection path;

(b) a dispersing component that receives the light from the collection lens and disperses the light into a plurality of light beams, as a function of a plurality of different discriminable characteristics of the light, said plurality of different discriminable characteristics being indicative of the plurality of different reporters;

(c) a plurality of light sensitive regions disposed on at least one detector;

(d) an imaging lens that focuses each of the plurality of light beams on said plurality of light sensitive regions, producing a respective image corresponding to each of the plurality of light beams, said plurality of light sensitive regions providing an output signal for each respective image, each output signal indicating those reporters present on the encoded bead; and

(e) means for processing the output signals to decode a sequence of the plurality of components.

47. The flow imaging system of Claim 46, wherein said means comprise a signal processor coupled to receive the output signals from said at plurality of regions.

48. The flow imaging system of Claim 46, wherein said means decodes a sequence of the plurality of components by:

(a) determining dispositions of the reporters on the encoded bead;

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(b) determining a signature of each reporter associated with the encoded bead based upon the dispositions of the reporters on the bead; and

(c) identifying each compound as a function of each reporter associated with the encoded bead.

49. The flow imaging system of Claim 46, wherein said means disregards all output signals relating to a reporter if signals from an identical reporter have already been analyzed for the encoded bead, and disregards all output signals for an encoded bead if said signals indicate that fewer than a predetermined number of reporters are associated with the encoded bead.

50. The flow imaging system of Claim 46, wherein said means de-convolves the output signals if said dispersing component convolves the plurality of light beams.

51. A flow imaging system for sequentially imaging and decoding a plurality of encoded beads entrained in a fluid, said encoded beads being associated with one or more compounds from among a plurality of different compounds, and with one or more reporters from among a plurality of different reporters, each compound being uniquely identified by at least one reporter, said flow imaging system comprising:

(a) a fluid system comprising an unanalyzed encoded bead supply, a detection volume, and an analyzed encoded bead reservoir, said fluid system being specifically adapted to hydrodynamically focus fluid moving from said unanalyzed encoded bead supply into said detection volume, such that encoded beads pass through said detection volume one at a time and into the encoded bead reservoir;

(b) means for collecting image data from each encoded bead passing though said detection volume, said image data being indicative of at least one characteristic of the encoded bead passing through the detection volume that is determinative of the reporters associated with the encoded bead; and

(c) a signal processor capable of decoding a plurality of encoded beads based on said at least one characteristic of the encoded beads collected by said means, to determine the compounds associated with each encoded bead that has been analyzed.

52. The flow imaging system of Claim 51, wherein said means for collecting image data from each encoded bead comprises:

(a) a collection lens disposed so that light traveling from the encoded beads passes through the collection lens and travels along a collection path;

(b) a dispersing component that receives the light from the collection lens and disperses the light into a plurality of light beams, as a function of a plurality different discriminable characteristics of the light, said plurality of different discriminable characteristics being indicative of the plurality of different reporters;

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(c) at least one pixilated detector;

(d) an imaging lens that focuses each of the plurality of light beams on said at least one pixilated detector, producing a respective image corresponding to each of the plurality of light beams, said at least one pixilated detector providing an output signal for each respective image, each output signal indicating those reporters present on the encoded bead; and

(e) a signal processor coupled to receive the output signals from said at least plurality of pixilated detectors, said signal processor processing the output signals to decode an identity of the compounds associated with each encoded bead analyzed.

53. The flow imaging system of Claim 51, wherein said signal processor is adapted to analyze said output signals to:

(a) determine locations of the reporters on the encoded bead,

(b) determine a signature of each reporter associated with the encoded bead based upon the locations of the reporters on the bead; and

(c) identify the compounds associated with each encoded bead as a function of each reporter associated with each encoded bead analyzed.

54. The flow imaging system of Claim 51, wherein said signal processor is adapted to disregard all output signals relating to a reporter if signals from an identical reporter have already been analyzed, and to disregard all output signals for an encoded bead if said signals indicate that fewer than a predetermined number of reporters are associated with the encoded bead.

55. The flow imaging system of Claim 51, wherein said signal processor is adapted to de-convolving the output signals if said dispersing component convolves the plurality of light beams.

56. The flow imaging system of Claim 51, wherein said dispersing component provides one respective image corresponding to a binding signal produced by the encoded bead itself.

57. The flow imaging system of Claim 56, wherein said signal processor is adapted to disregard all output signals for an encoded bead if said one respective image indicates that an encoded bead has not experienced a binding event.

58. A method of employing an oligo library encoded on beads for at least one of a DNA sequencing, a polymorphism analysis, and an expression analysis, said method comprising the steps of:

(a) providing an imaging system capable of decoding a sequence of encoded beads conveyed in a flow of fluid;

(b) generating a complete encoded bead library of N-mer oligos;

(c) selectively performing one of said DNA sequencing, said polymorphism analysis, and said expression analysis based on imaging data produced by imaging the encoded beads with the imaging system;

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(d) when the DNA sequencing is selected, amplifying genomic DNA using primers for extended sequences of interest;

(e) when the polymorphism analysis is selected, amplifying genomic DNA using primers for polymorphic regions of interest;

(f) when the expression analysis is selected, amplifying RNA using primers for genes of interest;

(g) hybridizing an amplified component produced by any of steps (d)-(f) in relationship to said encoded bead library;

(h) analyzing the encoded beads using the imaging data to identify oligo sequences of encoded beads hybridized in step (g); and

(i) constructing sequence contigs from the oligo sequences identified in step (h) to identify one of a genomic DNA sequence, a polymorphic allele, and an expressed gene.

59. The method of Claim 58, wherein said N-mer oligos comprises oligos having a length equal to ten.--

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